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# Dissociation of Saccade-Related and Pursuit-Related Activation in Human Frontal Eye Fields as Revealed by fMRI

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**Petit, L., V. P. Clark, J. Ingeholm, and J. V. Haxby.** Dissociation of saccade-related and pursuit-related activation in human frontal eye fields as revealed by fMRI. *J. Neurophysiol.* 77: 3386–3390, 1997. The location of the human frontal eye fields (FEFs) underlying horizontal visually guided saccadic and pursuit eye movements was investigated with the use of functional magnetic resonance imaging in five healthy humans. Execution of both saccadic and pursuit eye movements induced bilateral FEF activation located medially at the junction of the precentral sulcus and the superior frontal sulcus and extending laterally to the precentral gyrus. These findings extend previous functional imaging studies by providing the first functional imaging evidence of a specific activation in the FEF during smooth pursuit eye movements in healthy humans. FEF activation during smooth pursuit performance was smaller than during saccades. This finding, which may reflect the presence of a smaller pursuit-related region area in human FEF than the saccade-related region, is consistent with their relative size observed in the monkey. The mean location of the pursuit-related FEF was more inferior and lateral than the location of the saccade-related FEF. These results provide the first evidence that there are different subregions in the human FEF that are involved in the execution of two different types of eye movements, namely saccadic and pursuit eye movements. Moreover, this study provides additional evidence that the human FEF is located in Brodmann's area 6, unlike the monkey FEF which is located in the posterior part of Brodmann's area 8.

(Darby et al. 1996). These previous functional imaging studies all focused on different types of saccadic eye movements. To our knowledge, there is no published report of FEF activation during pursuit eye movements in humans.

The goal of the present study was to further investigate, with the use of fMRI, the anatomic location of the FEFs underlying both horizontal visually guided saccadic and pursuit eye movements. A second goal was to investigate the possible existence of two functional subregions in the human FEF, one for the control of saccadic eye movements and another for smooth pursuit eye movements. The present data have appeared previously in abstract form (Petit et al. 1996a).

## METHODS

Five right-handed healthy young adults (*S1–S5*), three females and two males, participated in this study. All were free of neurological or psychiatric illness, and there were no abnormalities on their structural magnetic resonance images (MRIs). All subjects gave written informed consent.

## Task design

fMRI scans were obtained while subjects alternately performed either visually guided saccadic or pursuit eye movements and baseline control tasks. During the saccadic task, subjects were asked to execute saccadic eye movements toward a visual dot. The dot appeared first at the primary central eye position for 500 ms, then jumped to different eccentric positions on the horizontal axis with a frequency of 2 Hz. The number of left and right saccadic eye movements were equated, with an average amplitude of 12° in both directions (range 5–20°). During the pursuit task, subjects were asked to follow a visual dot target starting at the primary central eye position and moving back and forth across the horizontal axis with a constant speed of 25°/s and with a maximal amplitude of 12° on both sides. The visual dot size was 0.4°. During the baseline control task, subjects were asked to keep the eyes open in total darkness, without any visual cue, and to avoid moving the eyes.

Visual targets were generated by a Power Macintosh computer (Apple, Cupertino, CA) with the use of SuperLab (Cedrus, Wheaton, MD) (Haxby et al. 1993) and were projected with a magnetically shielded liquid crystal display video projector (Sharp, Mahwah, NJ) onto a translucent screen placed at the feet of the subject. The subject was able to see the screen by the use of a mirror system. An RK-416PC pupil infrared eye tracking system (ISCAN, Cambridge, MA) was used to record the subject's eye movements outside the magnet to ascertain that the oculomotor tasks were performed correctly.

## INTRODUCTION

The frontal eye fields (FEFs) of monkeys were long thought to be responsible only for the control of saccadic eye movements (Goldberg and Segraves 1989). However, recent experiments have shown that the FEF also contributes to the control of smooth pursuit eye movements (Gottlieb et al. 1994; Lynch 1987). Thus the monkey FEF appears to be separated into two functional subregions: one that lies on the rostral bank of the arcuate sulcus and controls saccades, and another that is located more posteriorly in the arcuate sulcus and that controls pursuit (Gottlieb et al. 1993; Tian and Lynch 1996).

The site of the human FEF has been suggested by positron emission tomography (PET) studies of healthy humans performing saccadic eye movements. According to a recent review (Paus 1996), the human FEF appears to be located either in the vicinity of the precentral sulcus and/or in the depth of the caudalmost part of the superior frontal sulcus. Such a periprecentral location has been confirmed by other recent PET studies (O'Sullivan et al. 1995; Petit et al. 1996b; Sweeney et al. 1996) as well as by one study in which functional magnetic resonance imaging (fMRI) was used

### Imaging procedure

All imaging used a 1.5-T GE Signa magnet (Milwaukee, WI) with a standard head coil. Interleaved multislice gradient echo-planar image scanning was used to produce 26 contiguous, 5-mm thick axial slices covering the entire brain (field of view = 24 cm, repetition time = 3,000 ms, echo time = 40 ms, flip angle = 90°). Each subject performed four series contrasting saccade and control baseline tasks and four series contrasting pursuit and control baseline tasks, counterbalanced across subjects. For each series, subjects alternated 15 s of a control baseline task and 15 s of an oculomotor task. Each series consisted of 60 scans with a complete duration of 3 min. The scanner was in the acquisition mode for 12 s before each series to achieve steady-state transverse magnetization.

For all studies, high-resolution volume spoiled gradient recalled echo structural axial images were also acquired at the same locations as the echo planar images (repetition time = 13.9 ms, echo time = 5.3 ms, flip angle = 30°) to provide detailed anatomic information.

### Data analysis

Activity related to visually guided saccades and smooth pursuit was analyzed independently, relative to activity during the control task, with the use of an analysis of covariance (ANCOVA). Statistical analyses were restricted to brain voxels with adequate signal intensity by selecting voxels with an average intensity of  $\geq 20\%$  of the maximum value across voxels. Between-scan movement was corrected with Automatic Image Registration (AIR) software (Woods et al. 1993). For the ANCOVA, voxels that were activated during either saccadic or pursuit eye movements were identified by calculating correlations between the time series of MRI intensities in a single voxel and one idealized response function (Friston et al. 1994), reflecting contrast between one of the oculomotor tasks versus the control task. To increase statistical power, all four series of scans in each subject were analyzed together with the use of ANCOVA to factor out the series variance. A square wave that matched the time course of the experimental paradigm was convolved with a Gaussian model of the hemodynamic response (Friston et al. 1994; Maisog et al. 1995). All statistical results have a single voxel Z threshold of 2.33 (degrees of freedom corrected for correlation between adjacent time points). Statistical significance ( $P < 0.05$ ) of a region of activation was determined with the use of an analysis based on the spatial extent of each region to correct for multiple comparisons (Friston et al. 1994). For each subject, Z score maps and structural images were transformed into the standard stereotactic Talairach space (Talairach and Tournoux 1988) with the three-dimensional version of statistical parametric mapping (Friston 1995).

### RESULTS

All subjects showed bilateral periprecentral activations that correlated with the saccade task. The more medial and superior part of these activations was centered at the junction of the precentral sulcus and the superior frontal sulcus. The more lateral and superior part of these activations extended into the precentral gyrus. Table 1 provides stereotaxic coordinates of the maximum peak of the FEF activation for each subject. The location of the FEF activation was symmetrical for all five subjects.

Three of the five subjects (S1–S3) showed bilateral FEF activations correlated with the pursuit task, with the medial clusters located at the junction of the precentral sulcus and the superior frontal sulcus and an extension to the precentral

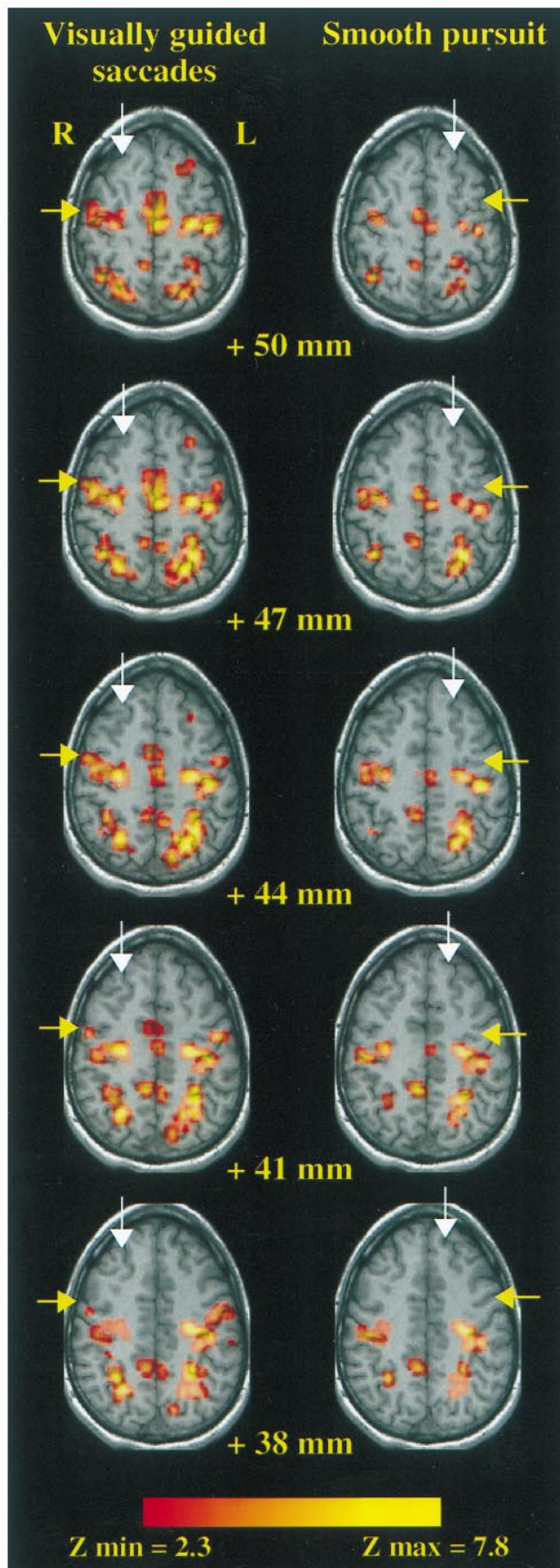
TABLE 1. Stereotaxic coordinates of the maximum frontal eye field activation for each subject during saccadic and pursuit eye movements as compared with the baseline control task

	Z Score	X	Y	Z	Ventrodorsal Extent of Activation (Z), mm
<i>A. Saccade vs. control</i>					
S1					
L	7.8	−25	−19	+44	+36 to +65
R	6.8	+27	−19	+41	+41 to +52
S2					
L	8.0	−21	−20	+43	+34 to +57
R	6.0	+26	−18	+45	+31 to +58
S3					
L	6.7	−26	−16	+42	+37 to +59
R	6.2	+26	−13	+48	+35 to +53
S4					
L	4.1	−38	−23	+52	+36 to +60
R	4.9	+43	−16	+52	+52 to +64
S5					
L	5.6	−38	−19	+54	+29 to +56
R	3.8	+43	−7	+56	+36 to +56
<i>n</i> = 5		X, mm		Y, mm	Z, mm
L		−30 ± 8		−19 ± 2	+47 ± 6
R		+33 ± 9		−15 ± 5	+48 ± 6
	Z Score	X	Y	Z	Ventrodorsal Extent of Activation (Z), mm
<i>B. Pursuit vs. control</i>					
S1					
L	5.2	−26	−21	+38	+38 to +45
R	4.0	+32	−18	+42	+42 to +52
S2					
L	3.9	−35	−23	+41	+37 to +41
R	2.4	+55	−12	+39	+39 to +45
S3					
L	5.3	−46	−10	+37	+31 to +47
R	3.8	+44	−3	+35	+35 to +46
S4					
L					
R	1.9*	+43	−25	+43	+35 to +48
S5					
L	4.2	−48	−7	+37	+35 to +50
R					
<i>n</i> = 4		X, mm		Y, mm	Z, mm
L		−39 ± 10		−15 ± 8	+38 ± 2
R		+43 ± 10		−14 ± 9	+40 ± 4

Values stated with  $\pm$  are means  $\pm$  SD. Coordinates (X, Y, Z) according to Talairach and Tournoux (1988). L, left; R, right. \* Not significant at the voxel Z threshold of 2.33.

gyrus for the inferior lower part of the activation. Pursuit-related activation in the left FEF was also present in S5, but in the left hemisphere only. A weak pursuit-related activation in the right-hemisphere FEF was observed in S4, although it failed to reach significance (Table 1). The pursuit-related FEF activation generally overlapped the saccade FEF activation seen during saccades. However, as illustrated for S1 (Fig. 1), the FEF activations during pursuit performance were smaller than those during saccades in terms of signal amplitude and spatial extent (Table 1).





The mean location of maximal pursuit-related activation was 10 mm lateral and 9 mm inferior to the mean location for maximal saccade-related activation (Table 1). Equivalent differences in location were found in the right and left activation. Figure 2 illustrates the location of maximal saccade- and pursuit-related FEF activation for the five subjects displayed on the mean structural MRI scan.

#### DISCUSSION

The execution of both visually guided saccadic and pursuit eye movements induced bilateral activations located medially at the junction of the precentral sulcus and the superior frontal sulcus and extending laterally to the precentral gyrus. This anatomic location corresponds to the human FEF that was identified previously in PET (for review: Paus 1996) and fMRI (Darby et al. 1996) studies. The present study extends previous works by providing the first functional imaging evidence of a specific FEF activation in the FEF during smooth pursuit eye movements in healthy humans. Previous pursuit-related FEF activation has been reported only in abstract form, with no information about the location and strength of these activations compared with saccade-related FEF activation (PET: Colby and Zeffiro 1990; fMRI: Berman et al. 1996).

In our study, the mean location of the maximal pursuit-related FEF activation was inferior and lateral to the mean location of the maximal saccade-related FEF activation. The present findings thus provide the first evidence that there are two distinct subregions in the human FEF that show increases in differential activity during the execution of two different types of eye movements, namely, saccades and smooth pursuit. Interestingly, two distinct functional subregions in the FEF have also been identified in the monkey for the generation of saccadic and pursuit eye movements, respectively (Goldberg and Segraves 1989; Gottlieb et al. 1994). In addition, in our study, FEF activation during pursuit eye movements appeared smaller than during saccades. This finding may reflect the presence of a smaller pursuit-related area in human FEF than the saccade-related FEF, which parallels results observed in the monkey (Gottlieb et al. 1994).

These results support the neurophysiological definition of the human FEF recently proposed by Paus (1996). According to this definition, the FEF would be identified as the caudal-most part of the frontal convexity that shows an increase in neuronal activity and, in turn, cerebral blood flow, during the execution of different types of eye move-

FIG. 1. Color-coded Z score maps from S1 illustrating bilateral frontal eye field (FEF) activation located at junction of precentral sulcus and superior frontal sulcus for the more medial part of the activation, and extending into the precentral gyrus for the lower part of the activation. Areas showing significantly increased magnetic resonance signal during visually guided saccadic (left) and pursuit (right) eye movements are displayed on the axial structural images of the subject. The five slice locations range from +50 to +38 mm above the bicommissural plane. Arrows: precentral sulcus (in yellow) and superior frontal sulcus (in white) for both hemispheres. L, left; R, right. Note also presence of supplementary eye fields and intraparietal activations during both oculomotor tasks in this subject.

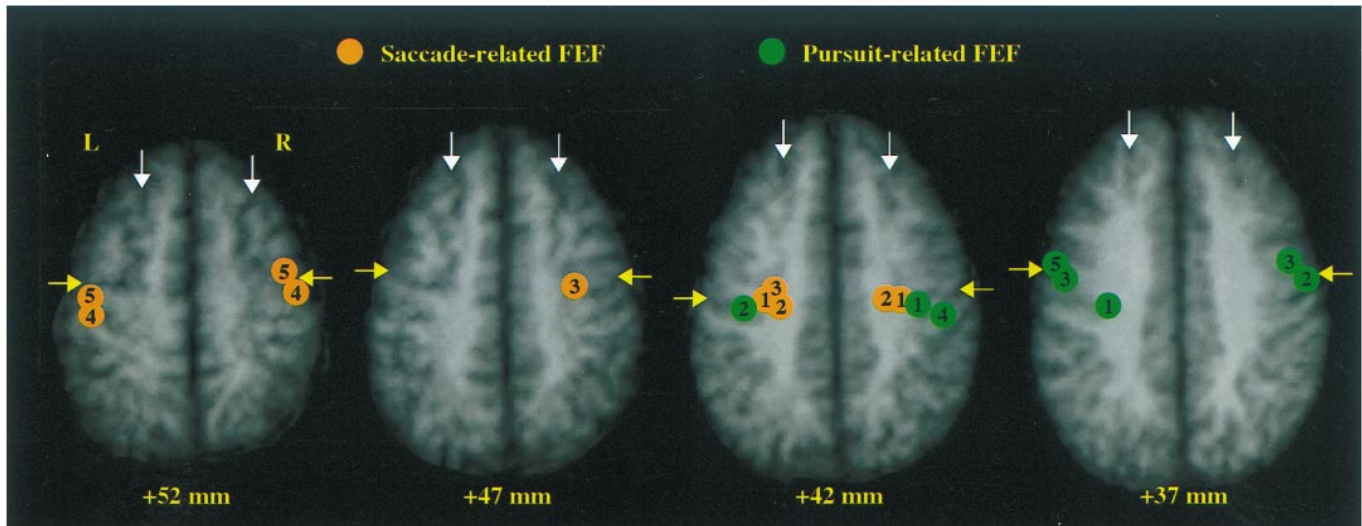


FIG. 2. Summary of location of both maximal saccade- and pursuit-related FEF activation for each subject displayed on mean spatially normalized axial structural images of the 5 subjects. The four slice locations range from +52 to +37 mm above bicommissural plane. Arrows: precentral sulcus (in yellow) and superior frontal sulcus (in white) for both hemispheres. L, left; R, right. Numbers 1–5: S1–S5.

ments. In the monkey, different neurons responsive to saccade, fixation, and pursuit tasks have been identified in the FEF (for review: Goldberg and Segraves 1990) leading to a well-circumscribed definition based on anatomic and functional properties. These studies have revealed that the monkey FEF lies on the rostral part of the arcuate sulcus and corresponds to the posterior part of Brodmann's area 8.

In contrast, functional brain imaging in humans has shown that the only common area of activation for saccades (for review: Fox et al. 1985; Paus 1996; Petit et al. 1993, 1996b), fixation (Petit et al. 1995), and pursuit (this study) tasks lies in the periprecentral region, which correspond to Brodmann's area 6 (Talairach and Tournoux 1988). It remains to be explained how different cytoarchitectonic areas, namely the periprecentral part of the human Brodmann's area 6 in humans and the posterior part of Brodmann's area 8 in the monkey, have similar functional properties.

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